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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/407,804	09/28/1999	JERRY PELLETIER	241/190	3252

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	19

DATE MAILED: 04/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/407,804	PELLETIER ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-14 and 33-72* is/are pending in the application.

4a) Of the above claim(s) *11,33-36,38,40-43,45 and 48-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,10,12-14,37,39,44,46,47,71 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 September 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1653.

Election/Restriction

Applicants' election with traverse of Group I, claim 9 (in part), 10 and 12-14 in Paper No. 18 is acknowledged.

The traversal is on the ground(s) that the requirement of the election of single nucleic acid sequence is improper because the notice 1192 OG 68 provides that "in most cases, up to ten (10) independent and distinct nucleotides sequence will be examined in a single application without restriction." Notably, it is only for "exceptional" cases that the number may be limited to less than 10. Further Applicants assert that there is nothing "exceptional" about the present sequences and claims that could justify limiting Applicants to a single sequence. This is not found persuasive because bacteriophage open reading frames 17, 19, 43, 102, 104 and 182 which are SEQ ID NO: 4, 5, 6, 7, 8 and 9 respectively do not encode same protein. Each is separably usable in the absence any one other polynucleotide and each is a different sequence and of a different length which makes them physically, chemically, biologically and structurally distinct. Thus each open reading frame sequence is patentably distinct and therefore requires restriction.

Regarding the rejoinder of claim 11 (Group II) with claims of Group I Applicants argue that searches based on nucleic acid and/or polypeptide must be performed with cross references between both types of sequences in order to be complete, and current sequence search tools are capable of automatically performing such searches, therefore there would be no additional search

burden on the Examiner. Applicants arguments are not found persuasive because searches only based on nucleic acid and/or polypeptide sequences is not a complete search to examine an invention. In addition to sequence database searches a literature search that includes patent and non-patent literature search completes the entire search. Therefore, as pointed out in the previous office action rejoinder of claim 11 to Group I claims would enlarge the search because Class 530 and subclass 350+, which is a large volume class, would be added to the search. Therefore, there would be an additional search burden. Moreover, inventions I and II are unrelated. Group I (claims 9, 10 and 12-14) is drawn to nucleic acid, and do not involve or require use of polypeptide as in Group II (claim 11) for its practice. Thus, each of Groups I, II has a mode of operation that is distinct from the other. The polypeptides and polynucleotides are distinct from their structure, and their physical, chemical and biological properties, thus one cannot be directly substituted for other. Furthermore, the search burden would be there as indicated by the different classification of each group.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11, 33-36, 38, 40-43, 45 and 48-70 are withdrawn under 37 C.F.R. § 1.142(b) from further consideration by the Examiner, as being drawn to a non-elected invention.

Claims 9, 10, 12-14, 37, 39, 44, 46, 47, 71 and 72 are pending and are under consideration in the instant application. Open reading frame 104 and SEQ ID NO: 8, which have been elected, are under examination.

Objection to the Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 21, lines 24 and 26; page 25, lines 31; page 45, lines 14,

28-34 and page 46, lines 1-6). Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 10, 12-14, 37, 39, 44, 46, 71 and 72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a bacteriophage 77 open reading frame (ORF) 104 full length sequence set forth in SEQ ID NO: 8; does not reasonably provide enablement for a portion of a sequence or fragments generated from any position located on the sequence of ORF 104 set forth in SEQ ID NO: 8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 9, 10, 12-14, 37, 39, 44, 46, 71 and 72 encompass an isolated nucleic acid sequence, at least 15 nucleotides in length that corresponds to a portion of bacteriophage 77 open reading frame (ORF) 104 (claim 9) that encodes a polypeptide which provides bacteria-inhibiting function (claim 10), wherein said sequence is transcriptionally linked with regulatory sequences enabling induction of expression of said sequence (claim 46), a recombinant expression vector comprising at least 24 nucleotides sequence corresponding to a portion of the sequence of ORF 104 set forth in SEQ ID NO: 8 wherein expression of said ORF is inducible (claims 12, 71, 72), a recombinant cell comprising a vector wherein said vector comprising at least 24 nucleotides sequence corresponding to a portion of the sequence of ORF 104 set forth in SEQ ID NO: 8 (claim 13), wherein the said vector is an expression vector and expression of said ORF is inducible (claim 14), the nucleic acid sequence of claim 9 comprising at least 45 nucleotides

sequence corresponding to a portion of the sequence of ORF 104 set forth in SEQ ID NO: 8 (claim 39), the nucleic acid sequence of the sequence of ORF 104 set forth in SEQ ID NO: 8 (claim 37, 44, 47).

The specification, however, only discloses cursory conclusions (see page 4), without data to support the findings, which state that the phage ORF products may be subportions of a larger ORF product that also binds the host target. There are no indicia that the present application enables the full scope in view of the nucleic acid sequences corresponding to a portion of a bacteriophage 77 open reading frame 104 as set forth in SEQ ID NO: 8 as discussed in the following stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is encompassed.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include: 1) the nature of the invention; 2) the breadth of the claims; 3) the predictability or unpredictability of the art; 4) the amount of direction or guidance presented; 5) the presence or absence of working examples; 6) the quantity of experimentation necessary; 7) the state of the prior art; and, 8) the relative skill of those skilled in the art;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

1) the nature of the invention:

The nature of the invention is defined by the claims, which include an isolated nucleic acid sequence of bacteriophage 77 open reading frame (ORF) 104 set forth in SEQ ID NO: 8, and at least 15 nucleotides in length that corresponds to a portion of bacteriophage 77 open reading frame (ORF) 104 that encodes a polypeptide which provides bacteria-inhibiting function. However the specification does not provide the information on the structure and function of the claimed portion of the sequence of said ORF 104.

2) the breadth of the claims:

The breadth of the claims is broad and encompasses an unspecified amount of variants regarding the bacteriophage 77 ORF 104 of SEQ ID NO: 8 as biological active fragments, which are not specifically described or demonstrated in the specification.

Claims 9 and 39 are directed to an isolated nucleic acid sequence, at least 15 and 45 nucleotides in length respectively that corresponds to a portion of bacteriophage 77 open reading frame (ORF) 104 that encodes a polypeptide, which provides bacteria-inhibiting function. No biological activities were attributed to the recited nucleic acid fragments and the structural information was limited (see specification page 10, lines 18-32). There is no disclosure about the bacteria-inhibiting activities of claimed fragments. Identification of these inhibitor ORFs is described in Example IV of the specification and inhibitory proteins derived from phage 77 ORFs were identified which inhibit bacterial growth in solid and liquid assays (Example V), however specification fails to provide any description or demonstration of a fragment of bacteriophage ORF of SEQ ID NO: 8 sequence having bacteria-inhibiting function. For these reasons, it requires undue experimentation to make the claimed invention, especially where in claims 9, 12 and 39, at least 15 nucleotides, 24 nucleotides and 45 nucleotides would have been included by the claims and for which the specification does not describe with particularity as to retention of function. Without any guidance or suggestions a skilled artisan would not be able to predict the structure of a fragment that would demonstrate the same activity as the activity of the ORF 104 sequence of SEQ ID NO: 8. Thus, for the reasons set forth above, undue experimentation is required to make and use the claimed fragments.

Claim 46 is directed to a nucleic acid sequence that encodes a polypeptide having bacteria-inhibiting function, wherein said sequence is transcriptionally linked with regulatory sequences enabling induction of expression of said sequence. Specification describes in Example IV a modified shuttle vector containing the arsenite inducible promoter, the arsR gene that enables induction of expression of ORFs. However, there is no disclosure of regulatory elements that are linked to the claimed fragments enabling induction of expression of said ORF fragments

and one skilled in the art would not have known the sequence of the regulatory element. For these reasons, it requires undue experimentation to make the claimed invention.

Claims 12, 71 and 72 are directed to a recombinant expression vector and claims 13 and 14 are directed to a recombinant cell comprising the fragment having at least 24 nucleotides in length of sequence of ORF 104, wherein the expression of said ORF is inducible. Specification defines 'inducible' at page 9 is meant that expression is absent or occurs at a low level until the occurrence of an appropriate environmental stimulus provides otherwise. For the present invention such induction is controlled by an artificial environmental change, such as by contacting a bacterial strain population with an inducing compound. While the specification in Example V describes and demonstrates that the expression of ORF 104 is inducible, there is no disclosure about the expression of claimed ORF fragments. For the reasons set forth above, undue experimentation is necessary to make and use the claimed fragments that retain the property of inducible expression of said ORF.

3) the predictability or unpredictability of the art;

The invention is highly unpredictable for the reasons set forth for factors 1 and 2 above.

As to factors 4 through 6,

4) the amount of direction or guidance presented;

5) the presence or absence of working examples; and

6) the quantity of experimentation necessary:

The claims are directed to an isolated nucleic acid sequence, at least 15 and 45 nucleotides in length respectively that corresponds to a portion of bacteriophage 77 open reading frame (ORF) 104 that encodes a polypeptide, which provides bacteria-inhibiting

function. However, the specification provides only a generic description of how a variety of fragments of ORFs can be generated (page 4), no specific guidance is provided on the generation of the fragments that demonstrate the biological activity of the ORF 104 fragment sequences. There are no working examples of these variants in the specification. While the specification in Example V describes and demonstrates that the ORF 104 set forth in SEQ ID NO: 8 encoding a polypeptide having bacteria-inhibiting function, there is no disclosure about the biological activities of the claimed fragments of ORF 104. Since the specification fails to provide sufficient guidance on the structure and function of the various fragments, it is necessary to have additional guidance on the identities of fragments to carry out further experimentation to assess their property of having bacteria-inhibiting function.

7) the state of the prior art; and,

8) the relative skill of those skilled in the art:

The prior art has shown a DNA encoding a Staphylococcus aureus protein, having 90.9% sequence identity to SEQ ID NO: 8 (see section below of 102(b) rejection), however, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the structure and function for various nucleic acid sequences to be considered enabling for variants/fragments for ORF 104.

In consideration of each of factors 1-8, it is apparent that there is undue experimentation because in summary, the scope of the claim is broad, the working example does not demonstrate the claimed variants, the guidance/the teaching in the specification is limited, and the outcome is unpredictable for the various modified forms, it is necessary to have additional guidance and to carry out further experimentation to assess the property of the variants. Therefore, due to large quantity of experimentation necessary to determine an activity or property of the disclosed ORF 104 and the fragments thereof, such that it can be determined how to use the claimed ORF of bacteriophage 77, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the specification fails to teach the skilled artisan how to make and use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 9, 12, 13 and dependent claims thereto 10, 37, 39, 44, 46, 47 and 71, 72 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9, 12 and 13 do not end in a period as required. See MPEP 608.01 (m). Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. "SEQ ID NO." should read as "SEQ ID NO:". Claims 10, 14, 37, 39, 44, 46, 47, 71, 72 are included in the rejection because they are dependent on rejected claim and do not correct the deficiency of the claim from which they depend.

Claims 9, 12, 13 and dependent claim 39 is indefinite because of the use of the term "corresponds" or "corresponding." The term "corresponds" or "corresponding" renders the claim indefinite, it is unclear what are the sequences that stand for as opposed to the sequence of SEQ ID NO: 8 of open reading frame 104.

Claims 9, 12, 13 are indefinite because of the use of the term "portion." The term "portion" renders the claim indefinite, it is not clear which portion of the nucleic acid sequence of SEQ ID NO: 8, whether it is 5' or 3' or in between. It is also not clear what is the position of that portion in relation to the sequence of SEQ ID NO: 8. Claims 10, 14, 37, 39, 44, 46, 47, 71,

72 are included in the rejection because they are dependent on rejected claim and do not correct the deficiency of the claim from which they depend.

Claims 14 and 72 are indefinite because of the use of the term "ORF". An acronym/abbreviation should be preceded by a full spelled out word. An insertion of "(ORF)" next to "open reading frame" in the independent claims is suggested.

Claims 37 and 44 are indefinite because they are identical. Also these claims are dependent to claim 9 and do not further limit the claim. Cancellation of claims 37 and 44 would overcome the rejection.

Claim 72 recites the limitation "said ORF" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 37, 44 and 47 are indefinite as there is no further limitation of the invention claimed in the independent claim 9 which they depend upon.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9, 10 and 39 are rejected under 35 U.S.C. 102 (b) as being anticipated by Black et al. (N_Geneseq_1101 database, Accession NO: AAT83989, August 21, 1997). Black et al. teach a DNA encoding a Staphylococcus aureus protein, having 90.9% sequence identity to SEQ ID NO: 8 (see alignment result). This sequence comprises corresponds to a portion of a bacteriophage 77 open reading frame 104 of SEQ ID NO: 8 (claims 9, 39) wherein the sequence

encodes a polypeptide which provides antibacterial action (see "cc" part in the document), thus anticipating claim 10 of the instant application.

Conclusion

No claim is allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr.Christopher Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

Rita Mitra, Ph.D.
April 3, 2002